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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/866,060 | 05/25/2001 | James W. Whittaker | HME/8134.003 | 4178 |

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EXAMINER

PAK, YONG D

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1652

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/866,060

Applicant(s)

WHITTAKER ET AL.

Examiner

Yong Pak

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10, 11 and 16-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10, 11 and 16-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

The amendment filed on February 3, 2003, canceling claims 9 and 12-15, amending claims 1, 4, 6, 8, 10 and 11 and adding claims 16-20, has been entered.

Claims 1-8, 10-11 and 16-20 are pending.

Rejections and/or objections not reiterated from previous Office action are hereby withdrawn.

Response to Arguments

Applicant's arguments filed February 3, 2003 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

✓ Claims 19-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "consume" is unclear. An enzyme does not consume its substrates. Enzymes bind to its substrates.

✓ Claims 17-18 recite the limitation "the temperature" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim.

✓ Claim 17 recites the limitation "the inducting" in line 1. There is insufficient antecedent basis for this limitation in the claim.

✓ Claim 18 recites the limitation "the induction" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-8, 10-11 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golightly et al. in view of Zamost et al.

Golightly et al. (U.S. Patent 6,277,612) teach DNA encoding a galactose oxidase linked to an *Aspergillus niger gla* signal peptide and an inducible promoter that regulates transcription of the sequence encoding the construct (claims 13 and 16, Columns 10-13 and Column 11). Golightly et al. also teach vectors comprising said DNA construct (claims 14-15 and 17-18 and Columns 13-17). Further, Golightly et al.

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also teach a method of producing the galactose oxidase using the vectors comprising the construct (claim 19 and Columns 10-17).

The difference between the reference of Golightly et al. and the instant invention is that the reference of Golightly et al. does not teach a DNA encoding the galactose oxidase linked to a methanol-inducible promoter and a galactose oxidase that is inactive.

Zamost et al. a method for producing a target polypeptide in a *Pichia* host cell wherein the polypeptide is under the control of a methanol-inducible promoter and a vector comprising the target polypeptide and the methanol-inducible promoter (claims 1 and 11 and Columns 3-10). Zamost et al. teach that methylotrophic yeasts such as a *Pichia*, are attractive candidates for use in recombinant protein production systems (Column 1, lines 19-65). One of ordinary skill in the art would recognize that proteins are usually inactive due to the presence of methanol in the culture medium.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use a methanol-inducible promoter to produce the protein in a *Pichia* host. The motivation of using a methanol-inducible promoter and a *Pichia* host is to effectively produce recombinant proteins. One of ordinary skill in the art would have had a reasonable expectation of success since *Pichia* hosts are routinely used in the art for the production of recombinant proteins and since methanol-inducible promoters have been used successfully in inducing proteins.

Applicants argue that there is no motivation to combine the reference of Golightly et al. and Zamost et al. because expression of galactose oxidase in an inactive form by

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induction by a methanol-inducible promoter results in an increased yield of galactose oxidase and increased homogeneity of the enzyme. The examiner disagrees.

It is well known in the art that expression of heterologous proteins wherein a methanol-inducible promoter is used to induce the protein leads to increased yields of the enzyme. The increased in the yield of the expressed protein is not unexpected. It is well known in the art that using methanol-inducible promoters in expressing proteins increases the yield of the protein (Zamost et al., background of the invention, Sakai et al. U.S. Patent 5,750,372, Columns 1-2). Applicants have not shown that the increased in yield of the expressed protein is due to it being expressed as an inactive form and rather than from using the methanol-inducible promoter. Also, one of ordinary skill in the art would recognize that proteins are usually inactive due to the presence of methanol in the culture. This inactive form of the protein is also not unexpected.

Claims 2 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golightly et al. in view of Zamost et al. as applied to claims 1, 3-8, 10-11 and 16 above, and further in view of Montague-Smith et al.

Golightly et al. and Zamonst et al. in combination teach a galactose oxidase expressed in an inactive form, as discussed above.

The difference between the combined teaching of Golightly et al. and Zamost et al. is that the references do not teach activating the inactive protein with an oxidant.

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Montague-Smith et al. teach that galactose oxidases can be activated by treatment with one-electro oxidants, such as ferricyanides (page 354, 1st and 2nd paragraph). Once the enzyme is activated by the oxidant, one of ordinary skill in the art would recognize that the enzyme would oxidize substrates and substrate like contaminants.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to activate the inactive galactose oxidase with the oxidant of Montague-Smith et al. The motivation of using the oxidant of Montague-Smith et al. is to activate the inactive protein. One of ordinary skill in the art would have had a reasonable expectation of success since Montague-Smith et al. successfully activated the protein.

Applicants argue that the activated protein of Montague-Smith et al. will degrade to the inactive form. The claims do not have limitations excluding possible degradation of the activated enzyme. Also, applicants have misinterpreted the reference. "is slowly reduced to a mixture of active and inactive forms, so that a large quantity of identical enzyme necessary for kinetic analyses cannot be maintained" refers to the state of the art prior to the teachings outlined in the reference. The paragraph following this statement "We have developed a method of rapidly activating or deactivating.." is what the reference teaches.

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No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 8:00 A.M. to 4:30 P.M weekdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

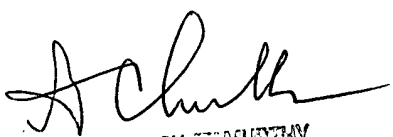
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Yong Pak
Patent Examiner

April 16, 2003


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